

## **CRD comments on draft COM testing strategy (strategy dated Nov 2010)**

**P 3 Para 3 line 3-4** CRD is not an example of a government agency. CRD is a directorate within HSE (HSE is a non departmental public body).

**P 3 Para 3 line 16-17** ....”mutagenic and genotoxic hazards (inherent properties of chemicals)”..... This could be interpreted, incorrectly, to mean that all chemicals possess these types of hazards.

**P 3 Para 4 line 26** ...”at that these times”.... A typo here.

**P 4 Para 5 Line 11** ....”internationally”.... Suggest replace with .....”international”.....

**P 5 Para 6 line 1-2** ....”Details of methodologies are not given”... However there is quite a bit of methodology discussion for the MNvit assay in paras 52-56.

**P 6 Para 11 line 28** Descendent is misspelt; it should be Descendant

**P7 para 13 line 23-24** ....”biological significance of genotoxicity tests”.... Suggest this is written ....”biological significance of genotoxicity results”....

**P8 para 18 line 28-29** “The *in vivo* genotoxicity testing strategy may also be required by regulatory authorities.....” We suggest it is more correct to say “*In vivo* genotoxicity testing may also be required by regulatory authorities.....”

**P9 para 19 line 10** “step genotoxicity testing strategy” sounds odd. Would “stepwise genotoxicity testing strategy” be better?

**P 9 para 19 line 12** “using” seems an odd word here

**P19 para 40 line 20 -21** “ A high sensitivity has been a priority of previous genotoxicity testing strategies recommended by the COM..” Suggest you clarify if it is still a COM priority.

**P 22 para 44 lines 1-2** With respect to the need or not for an independent confirmatory test. What does COM think about the need for an Ames test to include plate incorporation assay followed by pre-incubation assay?

**P22 para 44 line 8-10;** there appears to be something quite wrong with the wording here

**P27 para 57 line 18-21** “ It is important to include the use of chromosome specific centromeric probes with fluorescence in situ hybridisation (FISH) to assess the potential for aneuploidy. A wide range of FISH technologies exist for the analysis of clastogenic and aneugenic chromosome changes (Maierhofer et al., 2002).”

On p 24 at line 20 there is mention that detection of aneuploidy in the metaphase test **requires non-standard approaches**, as compared with the MNvit . However in the

above wording from p 27 there is no mention of the described approaches being non-standard.

**P27 para 57 line 22-25** “ One published evaluation of *in vitro* genotoxicity testing strategies reported that there was no scientific basis for including both a chromosomal aberration and micronucleus assay in addition to Ames and mouse lymphoma assays (Kirkland et al., 2005b).” It is not clear why this statement is included.

**P30 para 62 line 19-22** “Information from non-core tests described in this document may provide useful **additional** information on *in vitro* mutagenic hazards on a case-by-case basis.”

As the COM strategy provides guidance for all substances, including those with existing genotoxicity data (wording at start of section VI), the above statement does not seem to capture the scenario where existing non-core data may be the main basis for a genotoxicity assessment, ie in such a situation the non-core data would not be additional data but central to the assessment .

**P31 para 63 line 27** “**A** revised *in vivo* Stage 2 strategy based...” Would it not be clearer to write “**The** revised *in vivo* Stage 2 strategy based ...”

**P39-40 para 80** “ The Committee considers that the *in vivo* comet assay has appropriate sensitivity to detect chemicals **which induce both gene mutations and clastogenicity.**”

An important point: Would it be acceptable/correct to write?

“ The Committee considers that the *in vivo* comet assay has appropriate sensitivity to detect chemicals **which induce gene mutations and/or clastogenicity.**”

**Annex 2 Rodent comet assay.** “Valuable for detection of DNA damage in a wide range of tissues but gives no information modes of mutagenic action”.

An important point: if correct, it would be more informative for the wording be the same as for the *in vitro* comet assay ? , ie

“Can respond to a wide range of gene mutagens and clastogens but gives no information about modes of mutagenic action”